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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.			KIM, YOUNG J	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/622,010	MONFORTE, JOSEPH
	<b>Examiner</b>	<b>Art Unit</b>
	Young J. Kim	1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 02 May 2007.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-50 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-50 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- 1) Notice of References Cited (PTO-892)  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)  
 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date 6/8/07 *JM 6-25-07*
- 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date. \_\_\_\_\_.  
 5) Notice of Informal Patent Application  
 6) Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on May 2, 2007 has been entered.

### ***Information Disclosure Statement***

The IDS received on June 8, 2007 is acknowledged.

A signed copy of the PTO-1449 is enclosed herein.

### ***Claim Rejections - 35 USC § 102***

The rejection of claims 25-27, 33, 34, 37-45, and 50 under 35 U.S.C. 102(e) as being anticipated by Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000), made in the Office Action mailed on June 19, 2006 is withdrawn in view of the Amendment received on May 2, 2007.

Specifically, the rejection is withdrawn in view of the fact that none of the references teach producing a plurality of nucleic acid samples from a plurality of expressed RNA samples, and arraying said plurality of nucleic acid samples.

### ***Claim Rejections - 35 USC § 103***

The rejection of claims 1-13, 15-22, 24, 26, 27, 30-45, and 47-50 under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed

January 16, 2001, priority January 14, 2000) in view of Lockhart et al. (WO 97/10365, published March 20, 1997), made in the Office Action mailed on June 19, 2006 is withdrawn in view of the Amendment received on May 2, 2007.

Specifically, the rejection is withdrawn in view of the fact that none of the references teach producing a plurality of nucleic acid samples from a plurality of expressed RNA samples, and arraying said plurality of nucleic acid samples.

The rejection of claim 14 under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000) in view of Lockhart et al. (WO 97/10365, published March 20, 1997) as applied to claims 1-13, 15-24, 26, 27, 30-45, and 47-50 above, and further in view of Cho et al. (PNAS, August 14, 2001, vol. 98, no. 17, pages 9819-9823), made in the Office Action mailed on June 19, 2006 is withdrawn in view of the Amendment received on May 2, 2007.

Specifically, the rejection is withdrawn in view of the fact that none of the references teach producing a plurality of nucleic acid samples from a plurality of expressed RNA samples, and arraying said plurality of nucleic acid samples.

The rejection of claims 28, 29, and 46 under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000) in view of Lockhart et al. (WO 97/10365, published March 20, 1997) as applied to claims 1-13, 15-24, 26, 27, 30-45, and 47-50 above, and further in view of Nilsen (U.S. Patent No. 6,046,038, issued April 4, 2000) and Shuber (U.S. Patent No. 5,882,856, issued March 16, 1999), made in the Office Action mailed on June 19, 2006 is withdrawn in view of the Amendment received on May 2, 2007.

Specifically, the rejection is withdrawn in view of the fact that none of the references teach producing a plurality of nucleic acid samples from a plurality of expressed RNA samples, and arraying said plurality of nucleic acid samples.

The rejection of claims 28-32, 35-36, and 46-49 under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000) in view of Lockhart et al. (WO 97/10365, published March 20, 1997) Nilsen (U.S. Patent No. 6,046,038, issued April 4, 2000) and Shuber (U.S. Patent No. 5,882,856, issued March 16, 1999), made in the Office Action mailed on Office Action mailed on June 19, 2006 is withdrawn in view of the Amendment received on May 2, 2007.

Specifically, the rejection is withdrawn in view of the fact that none of the references teach producing a plurality of nucleic acid samples from a plurality of expressed RNA samples, and arraying said plurality of nucleic acid samples

***Rejection, New Grounds – Necessitated by Amendment***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-13, 15-22, 24-27, 30-45, and 47-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000) in view of Porkka et al. (Journal of Pathology, 2001, vol. 193, pages 73-79) and Lockhart et al. (WO 97/10365, published March 20, 1997).

Dooley et al. disclose a method of screening a candidate compound to identify a compound with a physiological effect on a biological sample, the method comprising the steps:

- a) contacting a biological sample with a candidate compound (minoxidil, column 10, lines 1-4);
- b) obtaining expressed RNAs from the sample (column 10, lines 4-5);
- c) arraying a plurality of nucleic acids corresponding to the plurality of expressed RNAs from the sample (column 10, line 8; column 3, lines 36-38 (informative arrays); column 5, lines 17-19);
- d) hybridizing a plurality of sequence probes derived from a sample treated with a candidate compound, so as to find other compounds that produce a similar biomarker response (column 10, lines 7-9);
- e) quantitating and detecting the hybridization signal, thereby identifying a compound that exerts a physiological effect on a biological sample (Figure 1, steps IV and V).

With regard to entering the quantitated hybridization signal into a database, the method of Dooley et al. compares the hybridization signal, which would necessarily require the entering of the hybridization signal into a computer which correlates the identified biomarkers with their expression level which is a database in its form (column 11, lines 7-21).

With regard to claim 3, Dooley et al. disclose employing control hybridization signal produced from the informative array (Figure 1, step III in view of Step V).

With regard to claim 12, Dooley et al. employ cell culture (Figure 1, step I; column 5, lines 34-35) and tissue (column 5, lines 32-33) as samples.

With regard to claim 13, Dooley et al. employ cell lines (column 5, line 34) as samples.

Art Unit: 1637

With regard to claims 15 and 16, Dooley et al. disclose that the samples are of eukaryotic (i.e., human or mammalian, column 4, lines 59) as well as *unicellular organisms*, plants, protists, and fungi (column 4, lines 60-64).

With regard to claims 4, 23, 24, 26, 27, 33, and 34, Dooley et al. disclose that the informative arrays are arrayed with isolated or purified immobilized nucleic acids, either native or synthetically created sequences, including PCR-amplification products (column 8, lines 48-54), such as oligonucleotide fragments, partial and full-length cDNA, expressed sequence tags (ESTs), including both partial and full-length ESTs, as well as RNA, DNA, or PNA (column 5, lines 1-9).

With regard to claim 37, Dooley et al. disclose that informative nucleic acid array is employed in identifying disease related genes (column 10, lines 45-57).

With regard to claims 38 and 39, Dooley et al. disclose that the array is a two-dimensional array (column 7, lines 43-44).

With regard to claims 40 and 41, Dooley et al. disclose that the nucleic acid can be arrayed on beads (column 7, lines 50-53; column 4, lines 14-15), as well as stating that “[o]ther platforms may be used, as desired.

With regard to claim 42, the array surface, in an embodiment, is disclosed as being glass (column 7, line 43), plastic (column 7, line 46), or silicon (column 8, line 33).

With regard to claim 43, the nucleic acid probes derived from cells, such as that which is generated from RNA (column 8, lines 39-42; column 9, line 22) or cDNA (column 9, line 5) is hybridized to the informative array.

With regard to claim 44, the nucleic acid probe is disclosed as being fluorescently labeled (column 8, line 41).

Art Unit: 1637

With regard to claim 45, claim 45 does not require that the method employ an amplifiable signal element be oligonucleotide, but rather further defines the Markush claim from which a detectable signal can be selected from. Since Dooley et al. disclose one of the Markush members (fluorescent label), claim limitations are met.

With regard to claim 50, Dooley et al. disclose comparison of the detected hybridization between samples (column 4, lines 24-28; Figure 1, steps I-III in view of V).

Dooley et al. do not employ their method for contacting a plurality of samples with a plurality of members of a compound library and generating an RNA sample from each of the plurality of the biological sample and arraying a plurality of nucleic acids produced from a plurality of expressed RNA samples to produce an array.

Dooley et al. do not disclose that each of the plurality of biological sample is contacted with a different member of the compound library (claim 2).

Dooley et al. do not explicitly disclose the use of control nucleic wherein the control biological sample comprises an untreated biological sample or a 0 time point sample (claim 5).

Dooley et al. do not explicitly disclose the step of quantitating hybridization signal wherein the signal differs qualitatively or quantitatively (claim 6), increased or decreased (claim 7), relative to the control hybridization signals.

Dooley et al. do not explicitly disclose the detection of the quantitated hybridization signals that differ from a control hybridization signal by performing at least one statistical analysis (claim 8), wherein the signal is increased or decreased at least one standard deviation (claim 9), at least two standard deviation (claim 10).

Dooley et al. do not explicitly disclose a method of using a plurality of nucleic acid arrays (claim 11).

Art Unit: 1637

Dooley et al. do not explicitly disclose a method comprising obtaining expressed RNA samples from at least 500 biological samples (claim 18), at least 1000 biological samples (claim 19), at least 10,000 biological samples (claim 20), each of which biological samples is treated with a different member of a compound library.

Dooley et al. do not explicitly disclose obtaining one or more expressed RNA samples by isolating total cellular RNA (claim 21).

Dooley et al. do not explicitly disclose obtaining one or more expressed RNA samples by isolating messenger RNA (claim 22).

Dooley et al. do not explicitly disclose pooling of amplification products for arraying (claim 30), wherein selective amplification amplifies between about 5 and about 100 polynucleotide sequences (claim 31), between about 10 and about 50 polynucleotide sequences (claim 32).

Dooley et al. do not disclose a method of employing housekeeping genes (claims 35 and 36).

Dooley et al. do not disclose a method of employing amplifiable signal element for detecting a plurality of defined sequence probes hybridized to the array (claim 46), involving chemiluminescent detection (claims 47-49).

Porkka et al. disclose a method of arraying differentially expressed mRNAs, wherein the differentially expressed mRNAs are made into cDNAs, then arrayed as a microarray (page 74, 1<sup>st</sup> column, bottom paragraph).

With regard to claims 2 and 17, Lockhart et al. disclose a method of employing a microarray for screening a plurality of compounds for identifying a candidate drug (page 8, line 30 through page 9, line 4).

With regard to claim 5, the control sample comprises an untreated biological sample (page 9, lines 5-7).

With regard to claims 6 and 7, Lockhart et al. the identification of candidate drug by the screening process is achieved via comparison of the expression profile from a test and a normal sample (page 9, lines 4-9; page 53, lines 22-24).

With regard to claims 8-10, Lockhart et al. disclose a method of detecting the signal difference by performing at least one statistical analysis (pages 58-60), wherein the differential expression measured which would necessarily include at least one or two standard deviations (page 62 through page 66; page 17, lines 2-4).

With regard to claims 21 and 22, Lockhart et al. disclose explicitly the steps involved in generating a RNA expression product (involved in Dooley et al.) which involves the steps of isolating total RNA and mRNA (page 4, lines 26-28; page 28, lines 17-20).

With regard to claim 30, Lockhart et al. disclose pooling (page 7, lines 10-12).

With regard to claims 31 and 32, depending on the number of the differentially expressed RNAs identified by the method of Dooley et al., the selective amplification would necessarily amplify between about 5 to about 100; or between about 10 and about 50 polynucleotide sequences.

With regard to claim 35, Lockhart et al. disclose the use of housekeeping genes for internal expression control (page 17, line 5; page 35, line 25 to page 36, line 5).

With regard to claim 36, the differentially expressed nucleic acid produced by treatment with a particular compound will necessarily be different the differentially expressed nucleic acid produced from a different compound (thus different second defined sequence probe). The use of housekeeping genes (or the first defined sequence probe) as an expression control, as demonstrated by Lockhart et al. will be same sequence however.

Art Unit: 1637

With regard to claims 47-49, Lockhart et al. disclose a method of detection involving enzyme and substrate (or ligand) (page 31, lines 21-27).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Dooley et al. with the teachings of Porkka et al. and Lockhart et al. to arrive at the claimed invention for the following reasons.

Applicants describe a classical microarray configuration, which is disclosed as below:

"the classical microarray formats known in the art (e.g. Thomas *et al.*) typically involve the arrangement of large numbers (e.g., hundreds or thousands) of defined "bait" sequences spatially arrayed on a solid phase surface, each in a unique addressable location, followed by application of a labeled nucleic acid sample (typically a collection of RNA or cDNA) to the microarray." (page 17, 3<sup>rd</sup> paragraph).

Applicants state that in contrast to such configuration, the claimed invention uses a novel variation of the classical microarray configuration, wherein the novel approach "flips" the standard microarray paradigm in that the nucleic acid samples are fixed on the solid phase support and the nucleic acid probe of defined sequence in solution is hybridized thereto.

However, it is respectfully submitted that such approach is neither novel nor unobvious as the advantage of such approach has been established, as demonstrated by Porkka et al., wherein the artisans explicitly state:

"Using cDNA array hybridization, the expression of thousands of genes can be studied simultaneously...Recently, protocols using cDNA microarrays on glass slides, or oligonucleotides on so called chips, together with fluorescent labeled probes, have been introduced...The chip technology is highly efficient, but requires expensive equipment for making the microarrays and for detecting the fluorescence signals." (page 73, 2<sup>nd</sup> column, 2<sup>nd</sup> paragraph, Porkka et al.)

Art Unit: 1637

Hence, while Dooley et al. disclose a method involving a microarray immobilized on a glass slide (or substrate), one of ordinary skill in the art would have clearly recognized an equivalent approach which would have been cost-effective. As Porkka et al. explicitly disclose the identification of the differentially expressed mRNAs followed by the immobilization of their encoded cDNAs, one of ordinary skill in the art would have been clearly motivated to employ any of the art recognized teachings for the art-recognized benefits (i.e., cost-effectiveness in arraying on glass slides), thereby arriving at the invention as claimed.

In at least one embodiment, Dooley et al. disclose a method of screening a plurality of compounds (such as drugs) in order to identify a candidate compound, wherein in that embodiment, a drug minoxidol is applied to a sample and its expression pattern is determined and compared against a control sample which had not been treated (*ut supra*). The differentially expressed genes (transcripts) were determined using the classical microarray containing a plurality of “bait” probes. However, the disclosure of Dooley et al. further takes the plurality of differentially expressed genes to make the informative array comprised of genes which are of particular interest. The informative array is then employed in testing a candidate compound by treating a sample with a candidate compound and detecting and comparing its expression pattern against the expression pattern produced from a control sample in order to determine whether the candidate compound is likely to produce a similar effect to that of, for example, minoxidol.

Dooley et al. disclose that the use of informative array provides the following advantages: “It is another advantage of the present invention for informative arrays to increase the likelihood that the gene sequences immobilized on it will be more informative (e.g., differentially expressed) in a desired application, *relative to a general array lacking a similar level of informative potential.*” (column 4, lines 19-24)

"Further more, it is another technical advantage of the present invention for informative array to permit *reduction in the total number of gene sequences immobilized on the informative array*. A reduction in the size of the informative array, due to the exclusion of non-informative genes from the list of candidate genes during the gene selection process." (column 4, lines 28-35).

Hence one of ordinary skill in the art at the time the invention was made would have been clearly motivated to employ the informative array of Dooley et al., via the array method disclosed by Porkka et al., for a cost-effective generation of an array produced by first identifying genes that are expressed based on a certain condition (such as treatment with a compound), wherein the identified genes are immobilized on the array, for the explicit advantage of increasing the likelihood that the gene sequences on the array will be more informative and that the array will permit reduction in the total number of gene sequences immobilized on the array. The reduction of in the total number of gene sequences immobilized on the array would have allowed one of ordinary skill in the art to clearly envision cost-effectiveness of conducting an experiment on such array, the benefit of which was commonly shared by both Dooley et al. and Porkka et al.

With regard to the teachings provided by Lockhart et al., the use of control samples, wherein the control sample is explicitly disclosed as being untreated sample, the use of housekeeping genes in an array for the purpose of quality control, and detection of differentially expressed genes above a certain threshold (or standard deviation), are techniques commonly practiced in the art as the desire to control quality of the expression profiles, and setting threshold from which to detect differential expression of genes are common across methods involving array of immobilized oligonucleotide probes.

With regard to use of plurality of nucleic acid array (claim 11), one of ordinary skill in the art would have been motivated to employ a plurality of informative array of Dooley et al. for testing different candidate compound of a compound library.

With regard to claims 18-20, drawn to the number of samples from which to obtain RNA samples, would have been obvious in view of the fact that each compound of a compound library being test would have required a different sample.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000) in view of Porkka et al. (Journal of Pathology, 2001, vol. 193, pages 73-79) and Lockhart et al. (WO 97/10365, published March 20, 1997) as applied to claims 1-13, 15-22, 24-27, 30-45, and 47-50 above, and further in view of Cho et al. (PNAS, August 14, 2001, vol. 98, no. 17, pages 9819-9823).

The teachings of Dooley et al. Porkka et al. and Lockhart et al. have already been discussed above.

Dooley et al., Porkka et al., and Lockhart et al. do not explicitly disclose treatment with members of the compound library recited in claim 14.

Cho et al. disclose a method involving treating a sample which overexpresses RI $\alpha$  gene with RI $\alpha$  antisense and determining the expression profile employing microarray (page 9819, 2<sup>nd</sup> column, 1<sup>st</sup>-3<sup>rd</sup> paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Dooley et al., Porkka et al., and Lockhart et al. with the teachings of Cho et al. to arrive at the claimed invention.

While Dooley et al., Porkka et al., and Lockhart et al. are not explicit in what type of compound or drug can be screened so as to identify a candidate compound or drug, as evidenced by Cho et al., antisense is one of many well-known compound which potentially has therapeutic use in treatment of certain conditions. In the word of Cho et al., the artisans state:

“Antisense oligonucleotides can selectively block disease-causing genes, and cancer genes that have been chosen as potential targets for antisense drugs to treat cancer.” (Abstract)

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to apply the teachings of Dooley et al., Porkka et al., and Lockhart et al. for screening a candidate compound or drug, including antisense, on the informative array produced by the combination of Dooley et al., Porkka et al., and Lockhart et al. with a reasonable expectation of success.

Claims 28, 29, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dooley et al. (U.S. Patent No. 6,635,423 B2, issued October 21, 2003, filed January 16, 2001, priority January 14, 2000) in view of Porkka et al. (Journal of Pathology, 2001, vol. 193, pages 73-79), and Lockhart et al. (WO 97/10365, published March 20, 1997) as applied to claims 1-13, 15-22, 24-27, 30-45, and 47-50 above, and further in view of Nilsen (U.S. Patent No. 6,046,038, issued April 4, 2000) and Shuber (U.S. Patent No. 5,882,856, issued March 16, 1999).

The teachings of Dooley et al., Porkka et al., and Lockhart et al. have already been discussed above.

Dooley et al., Porkka et al. and Lockhart et al. do not disclose a method of amplification involving multiplex PCR (claim 28), use of universal priming sequence (claim 29).

Art Unit: 1637

Dooley et al., Porkka et al., and Lockhart et al. do not disclose a method of signal amplification involving one or more of BDA, RCA, HSAM, RAM, and DNA dendrimer probe (claim 46).

Shuber discloses a multiplex amplification procedure involving the use of gene specific primers comprising a universal sequence (column 2, lines 54-60).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to employ the multiplex amplification method employed by Shuber in the amplification step of Dooley et al., Porkka et al., and Lockhart et al. for the motivation/advantage of simultaneously generating amplicons of multiple target nucleic acids which is known in the art as reducing time, contamination as well as reagent costs.

Nilsen discloses a method of detection involving DNA dendrimer probe (Figures 1A and 1B; column 9, lines 20-25).

Nilsen discloses that the use of dendrimer probe comprises arms organized at a surface layer with the capacity to bind the target as well as multiple labels, “which results in amplified signal” (column 9, lines 21-23).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, to combine the teachings of Nilsen with the teachings of Dooley et al., Porkka et al., and Lockhart et al. for the advantage of amplifying the signal produced by the target probe employed by Dooley et al. and Lockhart et al., achieving “50 to 100-fold signal enhancement,” (column 9, lines 62-63) the signal of which is critical in assays involving nucleic acid hybridization.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

### ***Conclusion***

No claims are allowed.

Art Unit: 1637

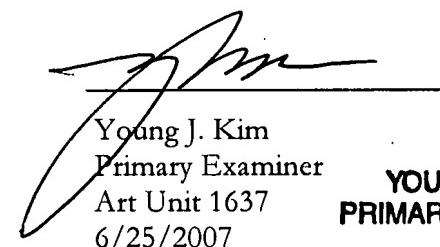
Applicant's arguments with respect to the previous rejections of record have been considered but are moot in view of the new ground(s) of rejection.

*Inquiries*

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to [Young.Kim@uspto.gov](mailto:Young.Kim@uspto.gov). However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.



Young J. Kim  
Primary Examiner  
Art Unit 1637  
6/25/2007

**YOUNG J. KIM**  
**PRIMARY EXAMINER**

YJK